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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ASTRAZENECA AB, AKTIEBOLAGET HÄSSLE, ASTRAZENECA LP, KBI INC. and KBI-E INC., Plaintiffs, v. IVAX CORPORATION, IVAX PHARMACEUTICALS, INC., IVAX PHARMACEUTICALS NV, INC., TEVA PHARMACEUTICAL INDUSTRIES LTD., TEVA PHARMACEUTICALS USA, INC. and CIPLA, LTD. Defendants.	Civil Action No. _____ **COMPLAINT AND CERTIFICATION PURSUANT TO LOCAL RULE 11.2**

JURISDICTION AND VENUE

1. This is an action for patent infringement and a declaratory judgment arising under the Patent and Food and Drug laws of the United States, Titles 35 and 21, United States Code. Jurisdiction and venue are based on 28 U.S.C. §§ 1331, 1338(a), 1391(b), 1391(c), 1400(b), 2201, 2202 and 35 U.S.C. § 271.

2. On information and belief, IVAX Corporation, IVAX Pharmaceuticals, Inc., IVAX Pharmaceuticals NV, Inc., Teva Pharmaceutical Industries Ltd., and Teva Pharmaceuticals USA, Inc. (jointly and severally "Teva") have been and are engaging in activities directed toward infringement of United States Patent No. 7,411,070 ("the '070 patent") by, *inter alia*, submitting an abbreviated new drug application designated ANDA No. 78-003 seeking FDA's approval to commercially manufacture, use and sell in the U.S. its proposed 20 mg and 40 mg Esomeprazole Magnesium Delayed-Release Capsules (hereinafter referred to as "Esomeprazole Magnesium Capsules") containing the active ingredient esomeprazole magnesium.

3. On information and belief, Cipla, Ltd. ("Cipla") has and will continue to aid, abet, induce, contribute to, engage in activities directed towards and otherwise participate in the infringement of the '070 patent by, *inter alia*, submitting a Drug Master File (DMF) seeking FDA approval to commercially manufacture, use and sell esomeprazole magnesium, supplying the bulk esomeprazole magnesium to be used in Teva's Esomeprazole Magnesium Capsules, importing and supplying the final Esomeprazole Magnesium Capsules to be marketed by Teva under ANDA No. 78-003, and otherwise aiding and abetting Teva in the preparation and submission of ANDA No. 78-003 and in its further preparations to commercialize Teva's Esomeprazole Magnesium Capsules upon FDA approval of ANDA No. 78-003.

4. In Teva's notice letter entitled "Notice of ANDA No. 78-003 Concerning Esomeprazole Magnesium Delayed-Release Capsules, 20 mg and 40 mg, With Paragraph IV Certification Concerning U.S. Patent No. 7,411,070" (hereinafter referred to as the "Notice of Certification"), Teva has indicated that it intends to market its Esomeprazole Magnesium Capsules before the expiration of the '070 patent.

5. Teva's submission of ANDA No. 78-003, Cipla's submission of the DMF, Cipla's supply of the active ingredient and drug product that is the subject oof Teva's ANDA , and service of Teva's Notice of Certification, indicates a refusal to change their current course of action.

6. There has been and is now an actual, justiciable controversy between Teva and Cipla on the one hand and Plaintiffs on the other hand as to whether Teva and Cipla have infringed, will infringe, have and will continue to induce, contribute to, engage in activities directed toward or otherwise aid and abet said infringement of the '070 patent.

THE PARTIES

7. Plaintiff AstraZeneca AB is a company organized and existing under the laws of Sweden, having its principal place of business at Södertälje, Sweden. AstraZeneca AB was a corporate name change from Astra Aktiebolaget.

8. Plaintiff Aktiebolaget Hässle ("Hässle") is a company organized and existing under the laws of Sweden, having its principal place of business at Mölndal, Sweden.

9. Plaintiff AstraZeneca LP is a limited partnership organized under the laws of Delaware, having its principal place of business at Wilmington, Delaware. AstraZeneca LP holds an approved New Drug Application from the United States Food and Drug Administration ("FDA") for an esomeprazole magnesium formulation which it sells under the name NEXIUM®.

10. Plaintiff KBI Inc. ("KBI") is a Delaware corporation having its principal place of business at Whitehouse Station, New Jersey.

11. Plaintiff KBI-E Inc. ("KBI-E") is a Delaware corporation having its principal place of business at Wilmington, Delaware. KBI and KBI-E have exclusive rights in the United States to the '070 patent.

12. On information and belief, defendant Ivax Corporation is a Florida corporation, having a principal place of business at 4400 Biscayne Blvd., Miami, Florida and having a place of business at 140 Legrand Avenue, Northvale, New Jersey. On information and belief, defendant Ivax Corporation is a wholly owned subsidiary of Teva Pharmaceuticals USA, Inc.

13. On information and belief, defendant Ivax Pharmaceuticals, Inc. is a wholly owned subsidiary of Ivax Corporation, having places of business at 4400 Biscayne Blvd., Miami, Florida and 140 Legrand Avenue, Northvale, New Jersey.

14. On information and belief, defendant Ivax Pharmaceuticals NV, Inc. is a wholly owned subsidiary of Ivax Pharmaceuticals, Inc., which in turn is a wholly owned subsidiary of Ivax Corporation, having a place of business at 140 Legrand Avenue, Northvale, New Jersey.

15. On information and belief, defendant Teva Pharmaceutical Industries Ltd. acquired Ivax Corporation, Ivax Pharmaceuticals, Inc. and Ivax Pharmaceuticals NV, Inc. on January 26, 2005.

16. On information and belief, defendant Teva Pharmaceutical Industries Ltd. is an Israeli corporation having a principal place of business at 5 Basel St., P.O. Box 3190, Petach Tikva 49131, Israel.

17. On information and belief, defendant Teva Pharmaceuticals USA, Inc. is a Delaware corporation, having a principal place of business at 1090 Horsham Road, P.O. Box 1090, North Wales, Pennsylvania 19454 and having places of business at 8 Gloria Lane, Fairfield, New Jersey 07004 and Two University Plaza, Suite 220, Hackensack, New Jersey 07601. On information and belief, defendant Teva Pharmaceuticals USA, Inc. is a wholly-owned subsidiary of Orvet UK, which is a wholly-owned subsidiary of Teva Pharmaceuticals Europe, which is a wholly-owned subsidiary of Teva Pharmaceutical Industries Ltd.

18. On information and belief, defendants Teva are doing business in New Jersey, have continuous and systematic contacts with New Jersey, have engaged in activities together related to the subject matter of this action and are subject to personal jurisdiction in this judicial district.

19. On information and belief, defendant Cipla, Ltd. is an Indian entity having a place of business at Mumbai Central, Mumbai 400 008, India.

20. On information and belief, defendants Cipla are doing business in New Jersey, have continuous and systematic contacts with New Jersey, have engaged in activities together related to the subject matter of this action and are subject to personal jurisdiction in this judicial district.

21. On information and belief Cipla supplies the active ingredient and the final product for Esomeprazole Magnesium Capsules that Teva intends to market prior to expiration of the ’070 patent.

CLAIM FOR RELIEF: ’070 PATENT

22. AstraZeneca AB, Hässle, AstraZeneca LP, KBI and KBI-E (collectively, “Plaintiffs”) reallege paragraphs 1-21, above, as if set forth specifically here.

23. The '070 patent (copy attached as Exhibit "A"), entitled "Form of S-omeprazole," was issued on August 12, 2008 to AstraZeneca AB upon assignment from the inventors Hanna Cotton, Anders Kronstrom, Anders Mattson and Eva Moller. The '070 patent is directed to, *inter alia*, magnesium salts of esomeprazole trihydrate and processes for preparing the claimed salts.

24. Plaintiff AstraZeneca AB has been and is still the owner of the '070 patent. The '070 patent will expire on May 25, 2018 and pediatric exclusivity relating to the '070 patent expires on November 25, 2018.

25. Teva's Notice of Certification notified Plaintiffs that it had submitted an Abbreviated New Drug Application ("ANDA") to the FDA under 21 U.S.C. § 355(j), seeking the FDA's approval to manufacture, use, offer to sell and sell Teva's Esomeprazole Magnesium Capsules as a generic version of the NEXIUM® product.

26. In the Notice of Certification, Teva notified Plaintiffs that, as part of its ANDA, it had filed a certification of the type described in 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV") with respect to the '070 patent. This statutory section requires, *inter alia*, certification by the ANDA applicant that the subject patent, here the '070 patent, "is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted . . . ." The statute (21 U.S.C. § 355(j)(2)(B)(iv)) also requires a Paragraph IV notice to "include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed." The FDA Rules and Regulations (21 C.F.R. § 314.95(c)) specify, *inter alia*, that a Paragraph IV notification must include "[a] detailed statement of the factual and legal basis of applicant's opinion that the patent is not valid, unenforceable, or will not be infringed." The detailed statement is to include "(i) [f]or each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is

not infringed" and "(ii) [f]or each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation."

27. On information and belief, at the time Teva's Notice of Certification was served, Teva was aware of the statutory provisions and regulations referred to in paragraph 26, above.

28. Teva's Notice of Certification does not provide a full and detailed explanation regarding non-infringement of the '070 patent claims, as is required by statute and regulation (see paragraph 26 above).

29. Teva's Notice of Certification, which is required by statute and regulation to provide a full and detailed explanation regarding invalidity (see paragraph 26 above), does not allege invalidity of all claims of the '070 patent

30. Teva's Notice of Certification, which is required by statute and regulation to provide a full and detailed explanation regarding unenforceability (see paragraph 26 above), does not address unenforceability or inequitable conduct of the '070 patent.

31. Teva's Notice of Certification fails to comply with the law, as specified in 21 U.S.C. § 355(j), and FDA rules and regulations, as specified in 21 C.F.R. § 314.95.

32. Teva has infringed the '070 patent under 35 U.S.C. § 271(e)(2) by filing its ANDA seeking approval from the FDA to engage in the commercial manufacture, use or sale of a drug claimed in this patent, or the use of which is claimed in the this patent, prior to the expiration of the '070 patent.

33. On information and belief, Teva's Esomeprazole Magnesium Capsules contain a magnesium salt of esomeprazole trihydrate as claimed by the '070 patent.

34. On information and belief, Teva's Esomeprazole Magnesium Capsules are manufactured by a process comprised of treating a magnesium salt of esomeprazole of any form with water as claimed by the '070 patent.

35. On information and belief, the manufacture, use and sale of Teva's Esomeprazole Magnesium Capsules infringes the '070 patent claims.

36. On information and belief, Cipla has and will, without authority, manufacture and import into the United States and/or use, offer to sell or sell within the United States the Esomeprazole Magnesium Capsules, or a material part thereof, which Teva then intends to offer for sale under ANDA No. 78-003, if approved, in violation of the '070 patent.

37. On information and belief, Cipla has and will continue to provide material information and physical product to Teva in connection with the preparation and submission of ANDA No. 78-003, which seeks approval to offer the Esomeprazole Magnesium Capsules for commercial sale in violation of the '070 patent. On information and belief, the information and product supplied by Cipla was relied upon and used by Teva in the submission of ANDA No. 78-003. By so doing, Cipla has and will knowingly and intentionally participate in, contribute to, aid, abet, engage in acts directed towards and/or induce the infringement of the '070 patent.

38. On information and belief, Cipla participated in, contributed to, aided, abetted, engaged in activities directed towards and/or induced infringement of the '070 patent. Therefore, Cipla is jointly and severally liable for any infringement of the '070 patent.

39. There has been and is now an actual justiciable controversy between Teva and Cipla on the one hand and Plaintiffs on the other hand as to whether Teva and Cipla have infringed, will infringe, or have contributed to, induced, aided and/or abetted infringement of or will contribute to, induce, aid and/or abet infringement of the '070 patent by the acts stated

above. This is so because Teva and Cipla have and will continue to, without altering course, engage in and make meaningful preparation to engage, in the infringing acts stated above.

WHEREFORE, Plaintiffs respectfully request the following relief:

(a) A judgment declaring that the effective date of any approval of Teva's ANDA under Section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355(j)) for the drug product "Esomeprazole Magnesium Capsules" must be later than November 25, 2018, the expiration date of the '070 patent, including pediatric exclusivity relating to the patent, that is infringed;

(b) A judgment declaring that the '070 patent remains valid, remains enforceable and has been infringed by Teva and/or Cipla if the Esomeprazole Magnesium Capsules are imported into, made, used, offered for sale or sold in the United States prior to the expiration of the '070 patent;

(c) A judgment declaring that Teva has not complied with the requirements of 35 U.S.C. § 271(e)(2), 21 U.S.C. § 355(j)(2)(A)(vii)(IV), 21 U.S.C. § 355(j)(2)(B)(iv), 21 C.F.R. § 314.94 and 21 U.S.C. § 314.95;

(d) A permanent injunction against any infringement by Teva and/or Cipla of the '070 patent;

(e) A judgment that Teva's and/or Cipla's conduct is exceptional;

(f) Attorneys' fees in this action under 35 U.S.C. § 285;

(g) Costs and expenses in this action; and

(h) Such other relief as this Court may deem proper.

Respectfully Submitted,

Date: October 9, 2008

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CERTIFICATION PURSUANT TO L. CIV. R. 11.2

Pursuant to Local Civil Rule 11.2, I hereby certify that the matter in controversy is the subject of the following actions:

ASTRAZENECA AB; AKTIEBOLAGET HÄSSLE; ASTRAZENECA LP; KBI INC.; and KBI-E INC. v. RANBAXY PHARMACEUTICALS, INC., RANBAXY INC., RANBAXY LABORATORIES LTD., IVAX CORPORATION, IVAX PHARMACEUTICALS NV, INC., IVAX PHARMACEUTICALS, INC., TEVA PHARMACEUTICALS INDUSTRIES, LTD., TEVA PHARMACEUTICALS USA, ZENITH LABORATORIES, INC., 3:05-cv-05553-JAP-TJB (Consolidated) (District of New Jersey).

ASTRAZENECA AB; AKTIEBOLAGET HÄSSLE; ASTRAZENECA LP; KBI INC.; and KBI-E INC. v. DR. REDDY'S LABORATORIES, LTD.; and DR. REDDY'S LABORATORIES, INC., 3:08-cv-00328-JAP-TJB (District of New Jersey).

ASTRAZENECA AB; AKTIEBOLAGET HÄSSLE; ASTRAZENECA LP; KBI INC.; and KBI-E INC. v. TEVA PARENTERAL MEDICINES, INC.; and TEVA PHARMACEUTICAL INDUSTRIES, LTD., 3:08-cv-02014-JAP-TJB (District of New Jersey).

IVAX PHARMACEUTICALS, INC. v. ASTRAZENECA AB; and MERCK & CO., INC., 3:08-cv-02165-JAP-TJB (District of New Jersey).

DR. REDDY'S LABORATORIES, LTD.; and DR. REDDY'S LABORATORIES, INC. v. ASTRAZENECA AB; AKTIEBOLAGET HÄSSLE; ASTRAZENECA LP; and MERCK & CO., INC. 3:08-vc-02496-JAP-TJB (District of New Jersey).

Date: October 9, 2008

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EXHIBIT A

US007411070B2

(12) United States Patent
Cotton et al.

(10) Patent No.: US 7,411,070 B2
(45) Date of Patent: *Aug. 12, 2008

(54) **FORM OF S-OMEPRAZOLE**

(75) Inventors: **Hanna Cotton**, Södertälje (SE); **Anders Kronström**, Södertälje (SE); **Anders Mattson**, Södertälje (SE); **Eva Möller**, Södertälje (SE)

(73) Assignee: **AstraZeneca AB**, Sodertalje (SE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **10/672,936**

(22) Filed: **Sep. 25, 2003**

(65) **Prior Publication Data**

US 2005/0075369 A1 Apr. 7, 2005

Related U.S. Application Data

(60) Continuation of application No. 10/076,711, filed on Feb. 14, 2002, now Pat. No. 6,677,455, which is a division of application No. 09/077,719, filed as application No. PCT/SE98/00974 on May 25, 1998, now Pat. No. 6,369,085.

(30) **Foreign Application Priority Data**

May 30, 1997 (SE) 9702065

(51) **Int. Cl.**
C07D 401/12 (2006.01)
A61K 31/4439 (2006.01)

(52) **U.S. Cl.** **546/273.7**; 514/338

(58) **Field of Classification Search** 514/338; 546/273.7

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,255,431	A		3/1981	Junggren et al.	424/263
4,738,974	A	*	4/1988	Brandstrom	514/338
4,786,505	A		11/1988	Lovgren et al.	424/468
5,530,160	A		6/1996	Nore et al.	562/571
5,676,884	A		10/1997	Tiers et al.	252/582
5,690,960	A	*	11/1997	Bengtsson et al.	514/338
5,693,818	A	*	12/1997	Vion Unge	514/338
5,714,504	A	*	2/1998	Lindberg et al.	514/338
5,817,338	A		10/1998	Bergstrand et al.	424/468
5,877,192	A		3/1999	Lindberg et al.	514/338
5,900,424	A		5/1999	Källström et al.	514/338
6,369,085	B1		4/2002	Cotton et al.	514/338
6,677,455	B2		1/2004	Kronstrom et al.	
6,747,155	B2		6/2004	Kronstrom et al.	

FOREIGN PATENT DOCUMENTS

CN	1136564		11/1996
DE	4 035 455		5/1992
EP	0005129		10/1979
EP	0124495		11/1984
EP	0247983		12/1987
EP	WO 95/01977	*	1/1995
IN	1344/DEL/98		5/1998
WO	9427988		12/1994
WO	9501977		1/1995
WO	9601623		1/1996
WO	9602535		2/1996

OTHER PUBLICATIONS

Japanese Chemical Society, Experimental Chemical Seminar. vol. 18. p. 55 (translation), 1958.*

An Introduction to Crystal Chemistry by Evans Cambridge At the Univ. Press, 1914.*

Erlandsson, P. Et al., "Resolution of the enantiomers of omeprazole and some of its analogues by liquid chromatography on a trisphenylcarbamoyl cellulose-based stationary phase", Journal of Chromatography, 532 (1990) 305-319.

von Unge, S. et al. "Stereochemical assignment of the enantiomers of omeprazole from X-ray analysis of a fenchyloxylmethyl derivative of (+)-(R)-omeprazole", *Tetrahedron Asymmetry*, vol. 8, No. 12, pp. 1967-1970 (1997).

An Introduction to Crystal Chemistry by Evans Cambridge at the Univ. Press, 1964.

Opposition filed by Ranbaxy Laboratories Limited against Indian Patent Application No. 1344/DEL/98.

Opposition filed by Torrent Pharmaceuticals Limited against Indian Patent Application No. 1344/DEL/98.

X-ray powder diffraction pattern of Mg-salt of S-omeprazole trihydrate depicted by Torrent obtained by method of WO 94/27988.

NDA 21-153/S-020 for Nexium® (esomeprazole magnesium) Delayed Release Capsule.

NDA 21-153/21-154 entitled "Medical Review(s)".

Statement with Exhibits A-C on Behalf of the Applicant, AstraZeneca AB, to the Opposition filed by Ranbaxy Laboratories Limited against Indian Patent Application No. 1344/DEL/98.

Statement with Exhibits A-D on Behalf of the Applicant, AstraZeneca AB, to the Opposition filed by Torrent Pharmaceuticals Limited against Indian Patent Application No. 1344/DEL/98.

Decision of the Pre-grant Opposition filed by Ranbaxy Laboratories Limited against Indian Patent Application No. 1344/DEL/98.

Decision of the Pre-grant Opposition filed by Torrent Pharmaceuticals Limited against Indian Patent Application No. 1344/DEL/98.

Notice of Allegation, dated Nov. 13, 2007, pursuant to the *Patented Medicines* (*Notice of Compliance*) *Regulations* with respect to Canadian Letters Patent No. 2,290,963.

* cited by examiner

Primary Examiner—Charanjit S Aulakh
(74) *Attorney, Agent, or Firm*—White & Case LLP

(57) **ABSTRACT**

The present invention relates to a novel form of the (−)-enantiomer of 5-methoxy-2[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole, i.e. S-omeprazole. More specifically, it relates to a novel form of the magnesium salt of the S-enantiomer of omeprazole trihydrate. The present invention also relates to processes for preparing such a form of the magnesium salt of S-omeprazole and pharmaceutical compositions containing it. Furthermore, the present invention also relates to new intermediates used in the process.

4 Claims, 5 Drawing Sheets

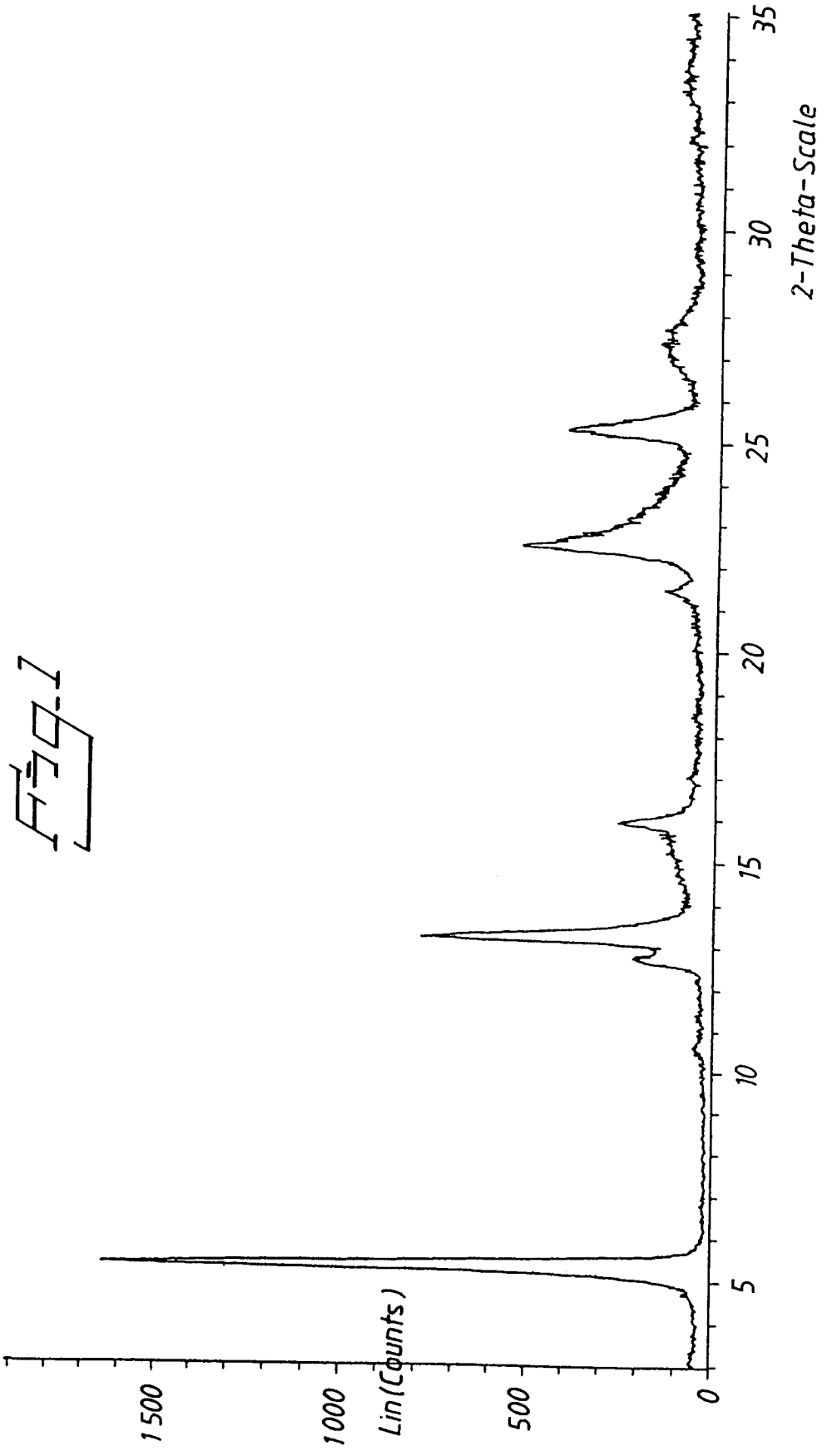

Fig 1

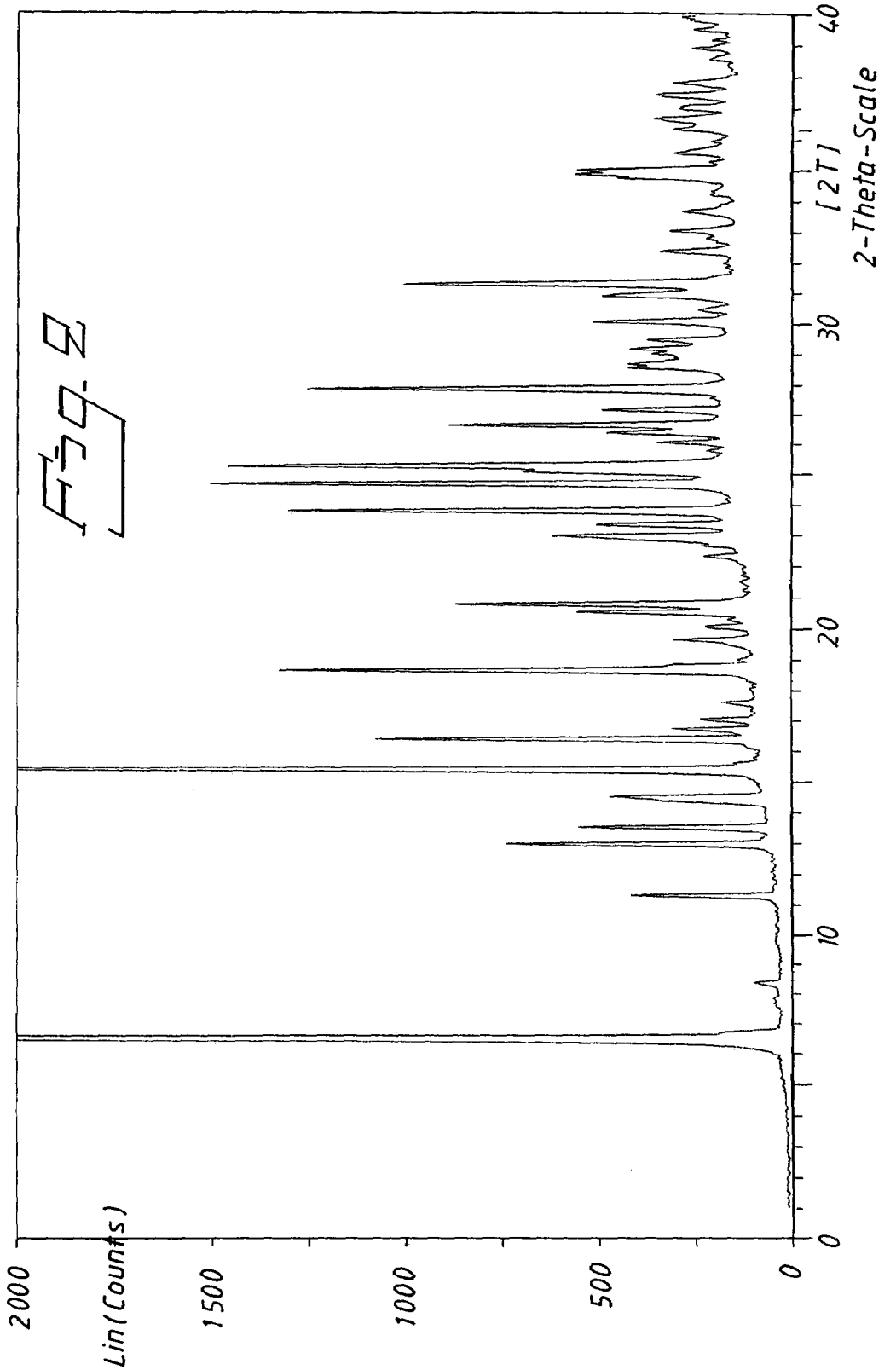
Fig. 2
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1000
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0
0
10
20
30
40
[2T]
2-Theta-Scale

Fig. 3

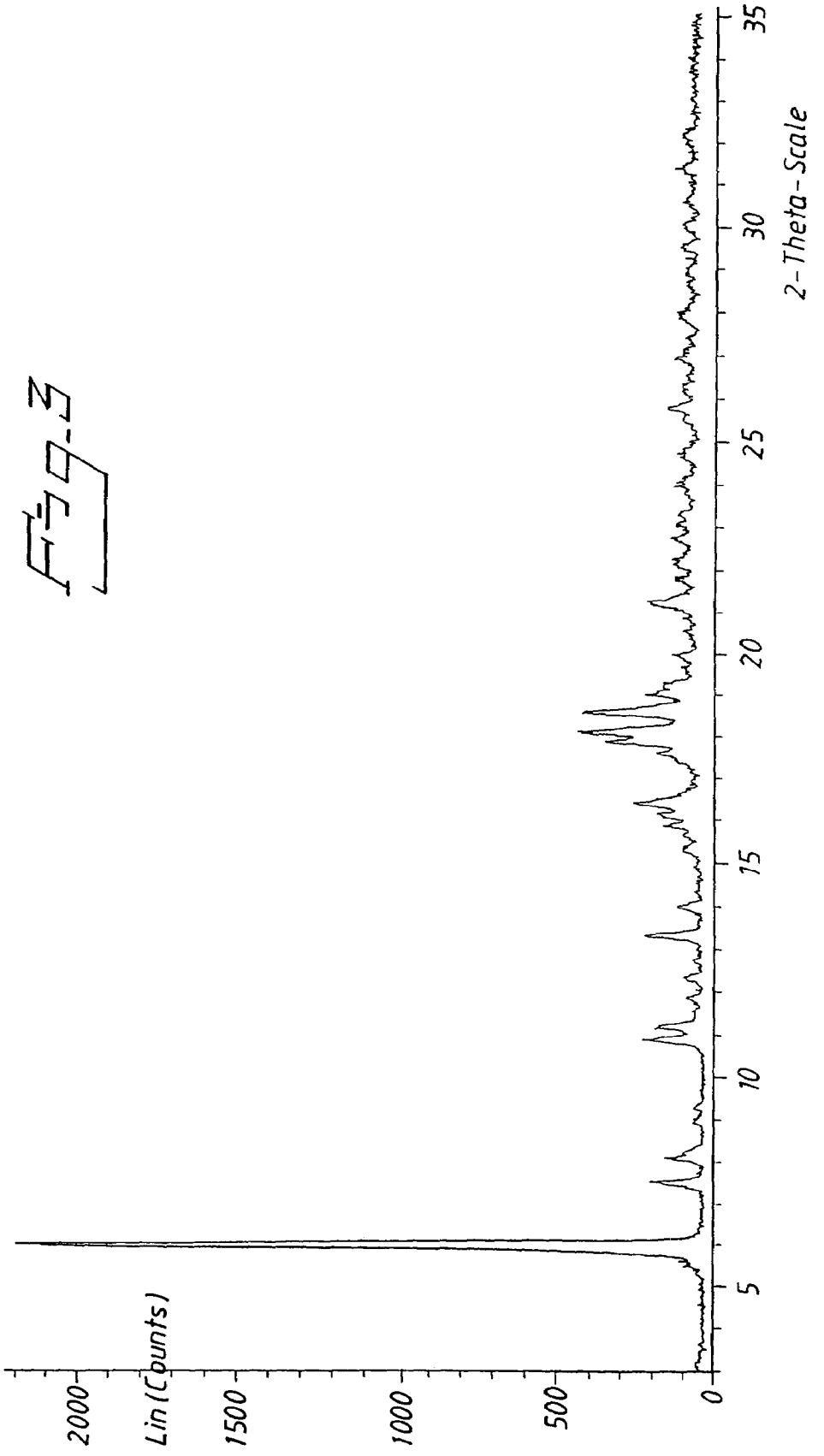
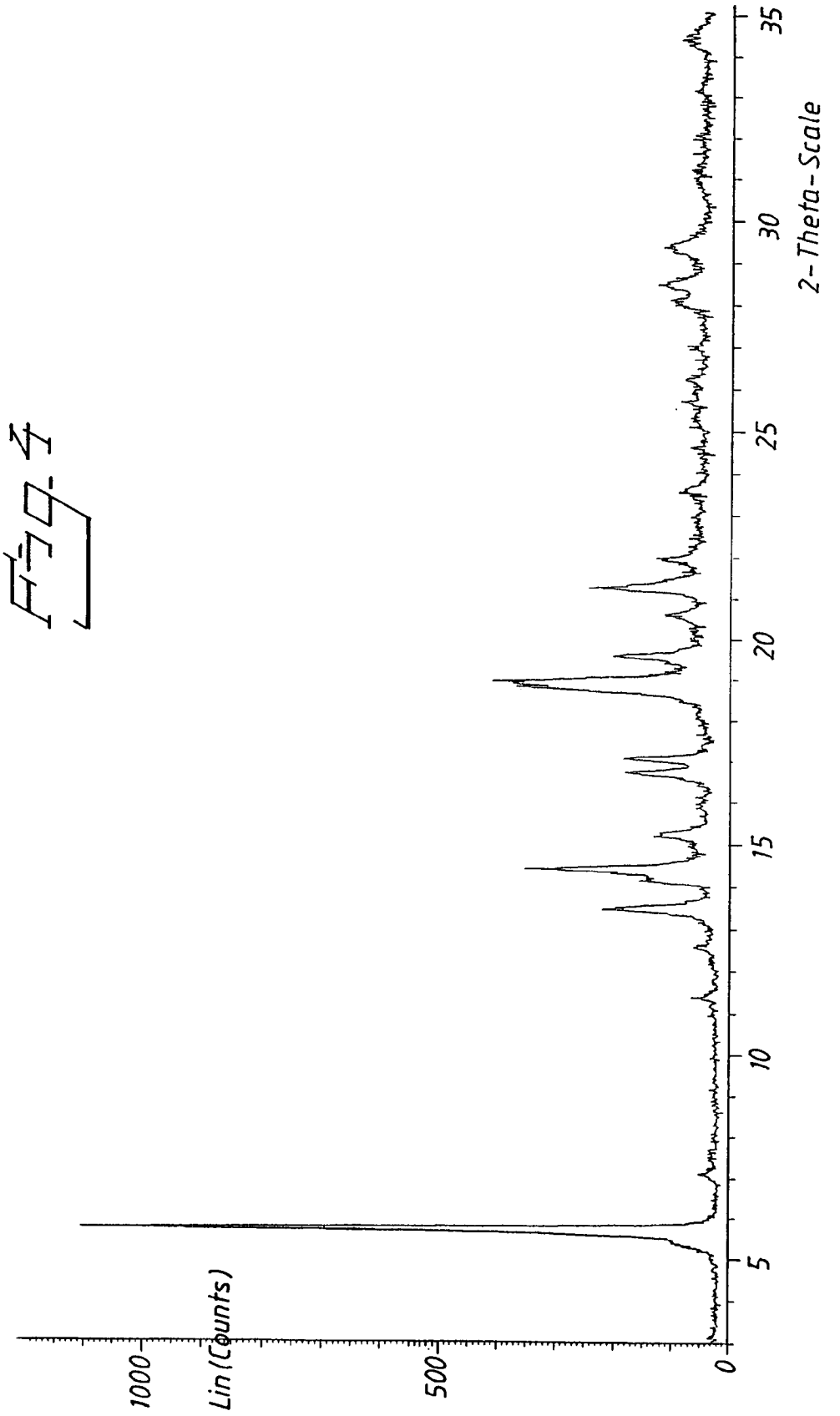


Fig. 4



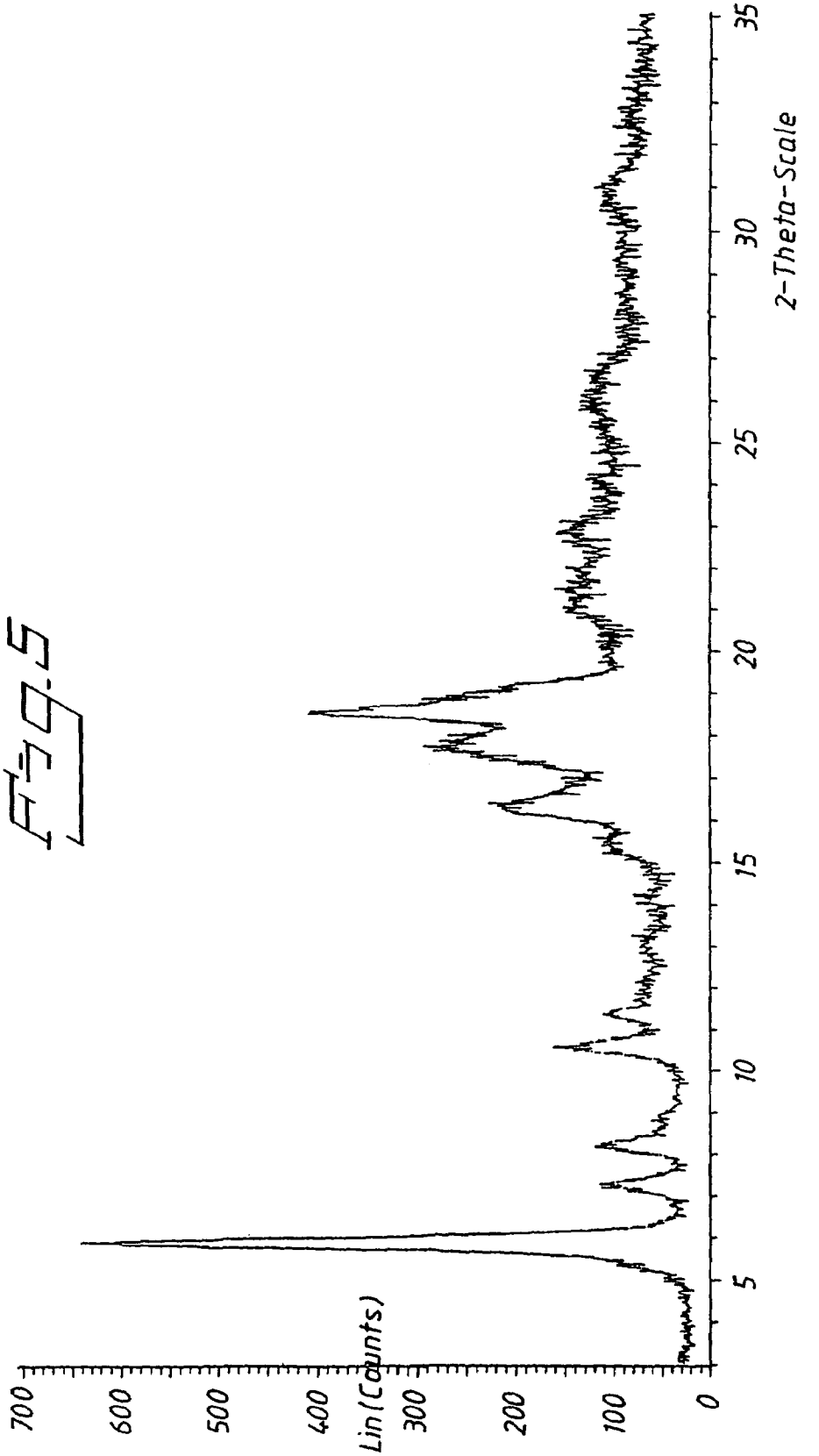

700
600
500
400
300
200
100
0
Lin (Counts)
5
10
15
20
25
30
35
2-Theta-Scale

FIG. 5

FORM OF S-OMEPRAZOLE

This application is a continuation of U.S. patent application Ser. No. 10/076,711, filed Feb. 14, 2002, now U.S. Pat. No. 6,667,455 which is a divisional of U.S. patent application Ser. No. 09/077,719, filed Jun. 8, 1998, now U.S. Pat. No. 6,369,085, which was the National Stage of International Application No. PCT/SE98/00974, filed May 25, 1998.

FIELD OF THE INVENTION

The present invention relates to a novel form of the (−)-enantiomer of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole, i.e. S-omeprazole. More specifically, it relates to a novel form of the magnesium salt of the S-enantiomer of omeprazole trihydrate. The present invention also relates to processes for preparing such a form of the magnesium salt of S-omeprazole and pharmaceutical compositions containing it. Furthermore, the present invention also relates to intermediates used in the process, and their preparation.

BACKGROUND OF THE INVENTION AND PRIOR ART

The compound 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole, having the generic name omeprazole, and therapeutically acceptable salts thereof, are described in EP 5129. The specific alkaline salts of omeprazole are disclosed in EP 124 495. Omeprazole is a proton pump inhibitor, i.e. effective in inhibiting gastric acid secretion, and is useful as an antiulcer agent. In a more general sense, omeprazole may be used for prevention and treatment of gastric-acid related diseases in mammals and especially in man.

Omeprazole is a sulfoxide and a chiral compound, wherein the sulfur atom being the stereogenic center. Thus, omeprazole is a racemic mixture of its two single enantiomers, the R and S-enantiomer of omeprazole, herein referred to as R-omeprazole and S-omeprazole. The absolute configurations of the enantiomers of omeprazole have been determined by an X-ray study of an N-alkylated derivative of the (+)-enantiomer in non-salt form. The (+)-enantiomer of the non-salt form and the (−)-enantiomer of the non-salt form were found to have R and S configuration, respectively, and the (+)-enantiomer of the magnesium salt and the (−)-enantiomer of the magnesium salt were also found to have R and S configuration, respectively. The conditions for the optical rotation measurement for each of these enantiomers are described in WO 94/27988.

Certain salts of single enantiomers of omeprazole and their preparation are disclosed in WO 94/27988. These compounds have improved pharmacokinetic and metabolic properties which will give an improved therapeutic profile such as a lower degree of interindividual variation.

WO 96/02535 discloses a process for the preparation of the single enantiomers of omeprazole and salts thereof, and WO 96/01623 discloses a suitable tableted dosage forms of for instance magnesium salts of R- and S-omeprazole.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** shows a X-ray powder diffractogram of the magnesium salt of S-omeprazole trihydrate prepared according to the present invention.

FIG. **2** shows a X-ray powder diffractogram of the potassium salt of S-omeprazole prepared and used in the present application (See examples 2 and 3)

FIG. **3** shows a X-ray powder diffractogram of a magnesium salt of S-omeprazole dihydrate prepared and used in the present application (See example 5)

FIG. **4** shows a X-ray powder diffractogram of a magnesium salt of S-omeprazole dihydrate which is a polymorph of the dihydrate shown in FIG. **3** (See Example 6). This magnesium salt of S-omeprazole dihydrate has been prepared and can be used in the preparation of the magnesium salt of S-omeprazole trihydrate according to the present invention.

FIG. **5** shows X-ray powder diffractogram of the magnesium salt of S-omeprazole prepared according to example A in WO 96/01623.

DESCRIPTION OF THE INVENTION

It has surprisingly been found that the magnesium salt of S-omeprazole occurs in a number of structurally different forms. It is an object of the present invention to provide a substantially pure magnesium salt of S-omeprazole trihydrate, hereinafter referred to as the compound of the invention. This trihydrate can be obtained as a well defined compound. The present invention also provides a process to obtain and a method of differentiating the magnesium salt of S-omeprazole trihydrate from other forms of magnesium salts of S-omeprazole.

The compound of the invention is advantageous because it is more stable than the corresponding magnesium salt compounds in prior art and is therefore easier to handle and store. The compound of the invention is also easier to characterize because it exists in a well defined state. Additionally, the compound of the invention is easier to synthesize in a reproducible manner and thereby easier to handle in a full scale production.

The magnesium salt of S-omeprazole trihydrate obtained according to the present invention is substantially free from magnesium salts of R-omeprazole. The magnesium salt of S-omeprazole trihydrate obtained according to the present invention is also substantially free from other forms of magnesium salts of S-omeprazole, such as the corresponding magnesium salt compounds described in prior art, and dihydrates used in the preparation of the trihydrate compound according to the present invention.

The compound of the invention is characterized by the positions and intensities of the major peaks in the X-ray powder diffractogram, but may also be characterized by conventional FT-IR spectroscopy. These characteristics are not exhibited by any other form of magnesium salt of S-omeprazole and accordingly, the magnesium salt of S-omeprazole trihydrate is easily distinguishable from any other crystal form of the magnesium salt of S-omeprazole disclosed in prior art. The compound of the invention is characterized by being highly crystalline, i.e. having a higher crystallinity than any other form of magnesium salt of S-omeprazole disclosed in the prior art. With the expression "any other form" is meant anhydrates, hydrates, solvates, and polymorphs or amorphous forms thereof disclosed in the prior art. Examples of any other forms of magnesium salt of S-omeprazole includes, but are not limited to, anhydrates, monohydrates, dihydrates, sesquihydrates, trihydrates, alcoholates, such as methanolates and ethanolates, and polymorphs or amorphous forms thereof.

The compound of the invention may also be characterized by its unit cell.

In a further aspect, the present invention provides processes for the preparation of the magnesium salt of S-omeprazole trihydrate which comprises;

a) treating a magnesium salt of S-omeprazole of any form, for example prepared according is to procedures known in the art such as Example A in WO 96/01623 which is incorporated herein by reference, with water at a suitable temperature for a suitable time. By a suitable temperature is meant a temperature which induces the transformation of starting material to product without decomposing any of these compounds. Examples of such suitable temperatures include, but are not limited to, room temperature and above. By a suitable time is meant a time that results in high conversion of the starting material into product without causing any decomposition of either compounds, i.e. results in a good yield. This suitable time will vary depending on the temperature used in a way well known to people in the art. The higher the temperature, the shorter time is needed to give the desired conversion. The amount of water is not crucial and will depend on the process conditions used. The magnesium salt of S-omeprazole trihydrate is thereafter separated from the aqueous slurry, for example by filtration or centrifugation and thereafter dried to constant weight; or

b) oxidizing 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]thio]-1H-benzimidazole, with an oxidizing agent and a chiral titanium complex, optionally in the presence of a base. The oxidation is carried out in an organic solvent, for example toluene or dichloromethane.

The crude product is converted to the corresponding potassium salt by treatment with a potassium source, such as methanolic potassium hydroxide or methanolic potassium methylate, followed by isolation of the formed salt.

The resulting potassium salt of S-omeprazole is thereafter converted to the corresponding magnesium salt by treatment with a magnesium source, such as magnesium sulfate in a lower alcohol, such as methanol. The solution is optionally filtered and the precipitation is initialized by addition of a non-solvent such as acetone. The product is filtered off and optionally washed with water and further processed as is described in a) above. Alternatively, the potassium salt may be treated with a magnesium source, such as magnesium sulfate in water, and isolation of the magnesium salt of S-omeprazole trihydrate, or any other conventional technique for transforming a potassium salt to the corresponding magnesium salt can be used and is within the scope of the present invention.

Yet a further aspect of the present invention is to provide a suitable intermediate used in the preparation of the compound of the invention, as well as a process for its preparation. The potassium salt of S-omeprazole is found to be such a suitable intermediate. The potassium salt of S-omeprazole may also be used as an active component of a pharmaceutical formulation to be used in the treatment of gastrointestinal diseases.

The compound of the invention, i.e. the magnesium salt of S-omeprazole trihydrate, prepared according to the present invention may be analyzed by XRPD, a technique which is known per se.

The amount of water in the magnesium salt of S-omeprazole trihydrate is determined by thermogravimetric analysis, a technique which is known per se.

The compound of the invention is effective as a gastric acid secretion inhibitor, and is useful as an antiulcer agent. In a more general sense, it can be used for prevention and treatment of gastric-acid related conditions in mammals and especially in man, including e.g. reflux esophagitis, gastritis, duodenitis, gastric ulcer and duodenal ulcer. Furthermore, it may be used for treatment of other gastrointestinal disorders

where gastric acid inhibitory effect is desirable e.g. in patients on NSAID therapy, in patients with Non Ulcer Dyspepsia, in patients with symptomatic gastro-esophageal reflux disease, and in patients with gastrinomas. The compound of the invention may also be used in patients in intensive care situations, in patients with acute upper gastrointestinal bleeding, pre- and postoperatively to prevent aspiration of gastric acid and to prevent and treat stress ulceration. Further, the compound of the invention may be useful in the treatment of psoriasis as well as in the treatment of Helicobacter infections and diseases related to these. The compound of the invention may also be used for treatment of inflammatory conditions in mammals, including man.

Any suitable route of administration may be employed for providing the patient with an effective dosage of the magnesium salt of S-omeprazole trihydrate, according to the invention. For example, peroral or parental formulations and the like may be employed. Dosage forms include capsules, tablets, dispersions, suspensions and the like.

It is further provided a pharmaceutical composition comprising the magnesium salt of S-omeprazole trihydrate according to the invention, as active ingredient, in association with a pharmaceutically acceptable carrier, diluent or excipient and optionally other therapeutic ingredients. Compositions comprising other therapeutic ingredients are especially of interest in the treatment of Helicobacter infections. The invention also provides the use of the magnesium salt of S-omeprazole trihydrate of the invention in the manufacture of a medicament for use in the treatment of a gastric-acid related condition and a method of treating a gastric-acid related condition which method comprises administering to a subject suffering from said condition a therapeutically effective amount of the magnesium salt of S-omeprazole trihydrate according to the invention.

The compositions of the invention include compositions suitable for peroral or parental administration. The most preferred route is the oral route. The compositions may be conveniently presented in unit dosage forms, and prepared by any methods known in the art of pharmacy.

In the practice of the invention, the most suitable route of administration as well as the magnitude of a therapeutic dose of the magnesium salt of S-omeprazole trihydrate according to the invention in any given case will depend on the nature and severity of the disease to be treated. The dose, and dose frequency, may also vary according to the age, body weight, and response of the individual patient. Special requirements may be needed for patients having Zollinger-Ellison syndrome, such as a need for higher doses than the average patient. Children and patients with liver diseases generally will benefit from doses that are somewhat lower than the average. Thus, in some conditions it may be necessary to use doses outside the ranges stated below, for example long term treatments may request lower dosage. Such higher and lower doses are within the scope of the present invention. Such daily doses may vary between 5 mg to 300 mg.

In general, a suitable oral dosage form of the compound of the invention may cover a dose range from 5 mg to 300 mg total daily dose, administered in one single dose or equally divided doses. A preferred dosage range is from 10 mg to 80 mg.

The compound of the invention may be combined as the active component in intimate admixture with a pharmaceutical carrier according to conventional techniques, such as the oral formulations described in WO 96/01623 and EP 247 983, the disclosures of which are hereby incorporated as a whole by reference.

Combination preparations comprising the magnesium salt of S-omeprazole trihydrate and other active ingredients may also be used. Examples of such active ingredients include, but are not limited to anti-bacterial compounds, non-steroidal anti-inflammatory agents, antacid agents, alginates and pro-kinetic agents.

The examples which follow will further illustrate the preparation of the compound of the invention, according to different process routes and including new intermediates. These examples are not intended to limit the scope of the invention as defined hereinabove or as claimed below.

EXAMPLES

Example 1

S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole Magnesium Salt Trihydrate

Water (157 kg) was added to the wet crystals of the magnesium salt of S-omeprazole, prepared according to Example 4, below. The mixture was heated to 38° C. with stirring and left for 3 hours. The crystals were filtered off and dried in vacuo. Yield: 31.6 kg.

X-ray powder diffraction analysis was performed on a sample of the crystals prepared above according to standard methods, which can be found in e.g. Kitaigorodsky, A. I. (1973), Molecular Crystals and Molecules, Academic Press, New York; Bunn, C. W. (1948), Chemical Crystallography, Clarendon Press, London; or Klug, H. P. & Alexander, L. E. (1974), X-Ray Diffraction Procedures, John Wiley and Sons, New York. The analysis gave the diffractogram depicted in FIG. **1**. The main peaks, with positions and relative intensities, have been extracted from the diffractogram in FIG. **1** and is given below in table **1**. The relative intensities are less reliable and instead of numerical values the following definitions are used.

% Relative Intensity	Definition
25-100	vs (very strong)
10-25	s (strong)
3-10	m (medium)
1-3	w (weak)
<1	vw (very weak)

Some additional very weak peaks found in the diffractogram have been omitted from table **1**.

TABLE 1

Positions and intensities of the major peaks in the XRP-diffractogram of the magnesium salt of S-omeprazole trihydrate.

d-value/Å	Relative Intensity
2.67	m
2.79	m
3.27	m
3.52	s
3.82	s
3.96	vs
4.14	m
5.2	m
5.6	m
6.7	vs
6.9	s

TABLE 1-continued

Positions and intensities of the major peaks in the XRP-diffractogram of the magnesium salt of S-omeprazole trihydrate.

d-value/Å	Relative Intensity
8.3	w
16.6	vs

Example 2

S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole Potassium Salt

A solution of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]thio]-1H-benzimidazole (15.4 g, 46.8 mmol) in toluene (70 ml) was heated to 50° C. and water (0.05 ml, 2.8 mmol) and D-(−)-diethyl tartrate (2.02 g, 9.82 mmol) were added. The reaction mixture was stirred for 20 minutes. Titanium(IV)isopropoxide (1.34 g, 4.68 mmol) was added and the reaction mixture was stirred for 45 minutes. The mixture was cooled to 30° C. and diisopropylethylamine (0.91 g, 7.01 mmol) was added followed by cumene hydroperoxide (9.52 g, 51.89 mmol). The resultant mixture was stirred at 30° C. for 3 hours. Methanol (40 ml) was added followed by potassium hydroxide (3.05 g, 46.8 mmol) in methanol (30 ml). Seed crystals were added and the reaction mixture was stirred at 35° C. overnight. The precipitated product was filtered off, washed with methanol and toluene and dried in vacuo. Yield: 9.74 g (54%).

Example 3

S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole Potassium Salt

Water (157.6 µl) was added to a solution of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]thio]-1H-benzimidazole in toluene (370 ml; 211.5 g/l) with a water content of 0.031% (w/w), followed by addition of D-(−)-diethyl tartrate (8.55 ml). The solution was heated to 50° C. and stirred at this temperature for 20 minutes. Titanium(IV) isopropoxide (7.15 ml) was added and reaction was left at 50° C. for 45 minutes. The temperature was lowered to 30° C. and diisopropylethylamine (6.2 ml) was added. Cumene hydroperoxide was added at an appropriate speed to maintain the temperature from 28° C. to 34° C. The temperature was raised to 35° C. after 2 hours and potassium methoxide (24.55 g) in methanol (222 ml) was added. The mixture was filtered after 14 hours and the crystals were washed with methanol:toluene (240 ml; 1:1) and methanol (120 ml) and dried. Yield: 79 g (74%), ee>99.9%.

$[\alpha]_D^{20}$=+28.7° (c=1%, water); Assay: 89% is S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl] sulfinyl]-1H-benzimidazole potassium salt (11% is methanol).

1H-NMR (200 MHz, DMSO-d6, δ ppm): 2.23 (s, 3H), 2.24 (s, 3H), 3.71 (s, 3H), 3.75 (s, 3H), 4.40 (d, 1H), 4.78 (d, 1H), 6.58 (dd, 1H), 7.00 (d, 1H), 7.35 (d, 1H), 8.25 (s, 1H).

The products from Examples 2 and 3 were analysed using X-ray powder diffraction as described in Example 1 and gave the diffractogram depicted in FIG. **2** and given below in Table

2. Some additional very weak peaks found in the diffractogram have been omitted from Table 2.

TABLE 2

Positions and intensities of the major peaks in the XRP-diffractogram of the potassium salt of S-omeprazole.

d-value/Å	Relative intensity
13.6	vs
10.6	vw
7.8	m
6.8	m
6.5	m
6.2	w
6.1	m
5.8	s
5.4	m
5.3	w
5.2	w
5.0	vw
4.75	m
4.71	w
4.52	w
4.42	w
4.32	w
4.27	m
3.98	vw
3.92	w
3.89	w
3.87	w
3.81	w
3.74	m
3.60	m
3.55	m
3.52	m
3.42	w
3.38	w
3.34	m
3.28	w
3.20	m
3.12	w
3.06	w
3.03	w
2.97	w
2.93	vw
2.89	w
2.85	m
2.76	w
2.71	vw
2.66	vw
2.58	w
2.57	w
2.56	w
2.52	vw
2.47	vw
2.45	vw
2.43	vw
2.40	vw
2.38	vw
2.31	vw

$\alpha 1$ = 1.54060 Å

Example 4

S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole Magnesium Salt

Methanol (148 kg) was added to S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole potassium salt (71 kg, methanol content=13%). $MgSO_4 \times 7H_2O$ (40 kg) was added to the mixture while stirring. After 70 minutes the mixture was filtered and the filtrate was washed with methanol (46 kg). The solution was concentrated to a volume of 100 liter, acetone (253 kg) was added and the resulting mixture was left for 4 hours. The precipitated product was filtered off, washed with acetone and water. The wet crystals were immediately used as is described in Example 1.

Example 5

S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole Magnesium Salt Dihydrate

5.0 g of the moist product from Example 4 with an approximate dry content of 74%, was dried in vacuum at 35° C. over night to yield 3.58 g (2.68 mmol) of S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole magnesium salt dihydrate, named Form B.

The product was analyzed using X-ray powder diffraction as described in Example 1, and the analyze gave the diffractogram depicted in FIG. **3** and given below in Table 3. Some additional peaks with low intensities found in the diffractogram have been omitted from Table 3.

TABLE 3

Positions and intensities of the major peaks in the XRP-diffractogram of the magnesium salt of S-omeprazole dihydrate, Form B.

d-value/Å	Relative Intensity
4.19	m
4.45	m
4.68	m
4.79	s
4.91	s
4.98	s
5.1	m
5.4	s
5.5	m
5.6	m
5.8	m
6.3	m
6.7	s
7.9	m
8.1	s
11.0	m
11.8	m
14.9	vs

Conversion of Magnesium Salt of S-omeprazole Dehydrate to Trihydrate

This material was subsequently processed to S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole magnesium salt trihydrate according to the procedure described for the moist substance in Example 1.

Example 6

S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole Magnesium Salt Dihydrate

A methanolic solution of S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium salt was prepared as is described in Example 4. Such a solution of S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium salt (1.86 g) in 5 ml methanol was concentrated by evaporation until 1.58 ml methanol remained. Then, a mixture of 1.6 ml water and 6.32 ml aceton was added. The solution was allowed to crystallize during 26 h at room temperature. The resulting crystals were filtered off and dried at

40° C. under reduced pressure giving 1.17 g of S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium salt dihydrate, named form A.

The product was analyzed using X-ray powder diffration as described in Example 1 and gave the diffractogram depicted in FIG. **4** and given below in Table 4. Some additional peaks with low intensities found in the diffractogram have been omitted from Table 4.

TABLE 4

Positions and intensities of the major peaks in the XRP-diffractogram of the magnesium salt of S-omeprazole dihydrate, Form A.

d-value/Å	Relative Intensity
3.04	s
3.14	s
3.18	m
4.05	s
4.19	s
4.32	m
4.54	s
4.69	vs
5.2	s
5.3	s
5.8	s
6.2	vs
6.6	s
15.5	vs

Example 7

S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole Magnesium Salt Trihydrate

22.0 g (29,1 mmol) of S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl) methyl]sulfinyl]-1H-benzimidazole potassium salt was dissolved in 40 mL of water. The solution was seeded with 0.11 g (0,1 mmol) S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole magnesium salt trihydrate. 22 mL (69,6 mmol) of $MgSO_4$ (aq) was added under a 3 h period. The slurry was filtered off and the precipitate was elutriated in water for approximately 30 minutes and the crystals were filtered off and dried (35° C., vacuum).

Yield: 9.15 g (11,6 mmol; 80%). The substance had a purity (HPLC):99.8 area %, Mg content: 3.40% (w/w) and ee: 99.8%.

The product was analyzed using X-ray powder diffraction and the result complies with FIG. **1** and Table 1.

Reference Example A

S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole Magnesium Salt

(The method used is in accordance with the method described in Example A in WO 96/01623)

Magnesium (0.1 μg, 4.5 mmol) was dissolved and reacted with methanol (50 ml) at 40° C. with a catalytic amount of methylene chloride. The reaction was run under nitrogen and was finished after five hours. At room temperature a mixture of the two enantiomers [90%(−)-isomer and 10%(+)-isomer] of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole (2.84 g, 8.2 mmol) was added to the magnesium methoxide solution. The mixture was stirred for 12 hours whereupon a small amount of water (0.1 ml) was added in order to precipitate inorganic magnesium salts. After 30 minutes stirring, these inorganic salts were filtered off and the solution was concentrated on a rotavapor. The residue was now a concentrated methanolic solution of the enantiomeric mixture (i.e. the title compound contaminated with the (+)-isomer), with an optical purity (enantiomeric excess, e.e.) of 80%. This mixture was diluted with acetone (100 ml) and after stirring at room temperature for 15 minutes, a white precipitate was obtained. Additional stirring for 15 minutes and thereafter filtration afforded 1.3 g (50%) of the title compound as white crystals. Chiral analyses of the crystals and mother liquor were performed by chromatography on an analytical chiral column. The optical purity of the crystals and mother liquor was found to be 98.4 e.e. and 64.4% e.e., respectively. Thus, the optical purity (e.e.) has been enhanced from 80% to 98.4% simply by crystallizing the Mg-salt from a mixture of acetone and methanol. The product was crystalline as shown by powder X-ray diffraction and the magnesium content was 3.44% as shown by atomic absorption spectroscopy. $[\alpha]_D^{20}=-131.5°$ (c=0.5%, methanol).

The product was analyzed using X-ray powder diffraction as described in Example 1 and gave the diffractogram depicted in FIG. **5** and given below in Table 5. Some additional very weak peaks found in the diffractograms have been omitted from Table 5.

TABLE 5

Positions and intensities of the major peaks in the XRP-diffractogram shown in FIG. 5.

d-value/Å	Relative Intensity
2.90	s
3.41	s
3.90	s
4.13	s
4.79	vs
5.00	vs
5.4	vs
5.7	s
6.3	s
6.8	s
7.8	s
8.4	vs
10.8	s
12.2	s
15.1	vs

The invention claimed is:

1. The magnesium salt of S-omeprazole trihydrate.

2. The magnesium salt of S-omeprazole trihydrate according to claim **1** represented by FIG. **1**.

3. A process for the preparation of the magnesium salt of S-omeprazole trihydrate according to claim **1** which comprises treating a magnesium salt of S-omeprazole of any other form with water.

4. A process for the preparation of the magnesium salt of S-omeprazole trihydrate according to claim **2** which comprises treating a magnesium salt of S-omeprazole of any other form with water.

* * * * *